Cystatin C: a promising misunderstood biomarker for the diagnosis of acute kidney injury

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To the Editor: Recently, we read with interest and pleasure Coca *et al.*'s[1] systematic review of the accuracy and reliability of serum and urinary biomarkers for the diagnosis and risk stratification of acute kidney injury (AKI). One of Coca *et al.*'s findings is that serum cystatin C (CysC) performed best for early as well as differential diagnosis of established AKI.

Timing for the detection of early-stage renal impairment is extremely important, especially in the therapeutic management of complex illness. In an acute condition, the absence of a reliable biomarker and the reliance on serum Cr (sCr) markedly delays the diagnosis and, consequently, the institution of therapy. Recently, research interest on the role of serum CysC in an intensive care unit (ICU) population has been stopped after the presumed association of CysC with inflammatory biomarkers in non-critically ill patients.[2]

We retrospectively reviewed all laboratory data referral to 1000 patients (611 mean, mean age 64.3 years) admitted in the ICU or the post-cardiac surgery intensive care unit (PCSICU). PCSICU population was submitted to extracorporeal circulation during cardiac surgical intervention. A total of 3993 samples tested contemporaneously for sCr, CysC and C-reactive protein (CRP) were selected (Table 1). Renal replacement therapy and known thyreopathy were exclusion criteria. No correlations between CysC vs CRP and sCr vs CRP were found either in ICU or in PCSICU. Moreover, we observed a well-known correlation between sCr and CysC in our entire population ($r = 0.739$, $P < 0.01$). Our results are encouraging for the resumption of the use of CysC for monitoring renal function in critically ill patients. Large multicenter studies in ICU populations are needed for definitive approval or not of serum CysC in early AKI diagnosis.

Table 1 | Mean and standard deviation (s.d.) of age, sCr, CysC and C-reactive protein (CRP) in our ICU population

	Age (years)	Cystatin C (0.55–0.95 mg/l)	CRP (<5 mg/100 ml)	Creatinine (0.7–1.2 mg/100 ml)
Women				
N	1662	1662	1662	1661
Mean	65.4	1.94	102.8	0.97
s.d.	16.1	1.14	95.5	0.75
Men				
N	2331	2331	2331	2328
Mean	58.9	1.786	105.7	1.16
s.d.	18.1	1.08	97.7	1.10
Total				
N	3993	3993	3993	3989
Mean	61.6	1.85	104.5	1.08
s.d.	17.6	1.10	96.8	0.97

CysC, cystatin C; ICU, intensive care unit; sCr, serum Cr.

1. Coca SG, Yalavarthy R, Concato J *et al.* Biomarkers for the diagnosis and risk stratification of acute kidney injury: a systematic review. *Kidney Int* 2008; **73**: 1008–1016.
2. Knight EL, Verhave JC, Spiegelman D *et al.* Factors influencing serum cystatin C levels other than renal function and the impact on renal function measurement. *Kidney Int* 2004; **65**: 1416–1421.

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Response to 'Cystatin C: a promising misunderstood biomarker for the diagnosis of acute kidney injury'

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We read with interest the letter in response to our systematic review and the new data from Ferrannini *et al.*,[1] which demonstrates that serum cystatin C is not correlated with C-reactive protein and is strongly correlated with serum creatinine. We agree that more studies investigating the utility of serum cystatin C in acute kidney injury (AKI) for critically ill patients should be conducted.

It is important, however, to not just correlate cystatin C concentration with serum creatinine concentration, as was presented in the study. The objective of the novel biomarker studies should be to replace serum creatinine or strengthen the current diagnostic and prognostic assessment along with serum creatinine. Thus, it is important to design studies and perform analyses, that would delineate other attributes of the new diagnostic tool rather than mimicking the diagnostic abilities of serum creatinine. For example, a study by Herget-Rosenthal *et al.*,[2] demonstrated that the rise in serum cystatin C preceded the rise in serum creatinine by 1.5 ± 0.6 days. This study also compared the performance of cystatin C against clinically meaningful end points, including the RIFLE definitions for AKI and dialysis-requiring AKI.